Largest Analysis to Date Examines Link Between Smoking and Outcomes in Acute Myeloid Leukemia

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CHICAGO–In patients with acute myeloid leukemia (AML), both current and former smoking is associated with worse treatment outcomes in treatment-naïve patients. A history of smoking is associated with molecular and cytogenetic risk factors, suggesting that it is tied to biological characteristics of the tumor rather than smoking-related comorbidities.

Previous studies have also shown an association between smoking and poor treatment outcomes in AML. The latest findings come from the largest analysis of smoking status and clinical characteristics in AML (abstract 7002). The work was presented at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting, held May 31–June 4 in Chicago.

Smoking is already known to increase relative risk of AML by 40% in active smokers, and by 25% in former smokers, leading the researchers to examine whether the practice could also impact treatment outcomes. They identified 561 patients (272 ever smokers, 289 never smokers) who were newly diagnosed between 2012 and 2017 at MD Anderson Cancer Center. Smokers were older (mean age, 69 years vs 63 years; $P < .0001$), more likely to be male (53% vs 45% female; $P < .0001$), and more likely to have secondary AML (27% vs 19%; $P = .028$).

In treatment-naïve patients, smoking was linked to higher relapse rates (43% vs 30%; $P = .0091$) and worse overall survival ($P < .0001$). In a multivariate analysis that took into account AML biologic characteristics and European Leukemia Net (ELN) 2017 risk stratification, smoking status was not significantly associated with outcomes. That finding suggested that biologic characteristics associated with smoking might explain the worse outcomes.

A univariate analysis showed a link between smoking and poor ELN risk ($P = .015$), complex karyotype (odds ratio [OR], 2.00; $P = .0002$), dysplasia (OR, 1.45; $P = .037$), *GATA2* mutation (OR, 0.27; $P = .029$), *mTP53* mutation (OR, 1.68; $P = .02$), *NPM1* (OR, 0.65; $P = .04$), and *FLT3-ITD* (OR, 0.75; $P = .027$).

After controlling for age, the associations remained significant for ELN risk, complex karyotype, and *GATA2*, but were lost for *NPM1*, *FLT3-ITD*, and *TP53*.

Although the study shows some interesting relationships, they are difficult to interpret due to the strong confounding effect of the bad biology of disease, according to one expert. “It’s a little difficult to separate out which came first, the chicken or the egg? Might there be an effect of smoking on developing worse biology in AML? That cannot be told from this study. But if you’re a smoker, your outcomes are worse, and there is a strong message that it’s a bad (idea) to smoke,” session moderator Gail Roboz, MD, told *Cancer Network*. Roboz is professor of medicine and director of the leukemia program at Weill Cornell Medicine.

“What would be incredibly interesting would be data showing what happens to clonal hematopoiesis of indeterminate potential (CHIP) in the setting of smoking and subsequent development of hematological malignancies, to see if there might be a pre-malignant mutational landscape that could possibly be worsened by smoking. That would be fascinating for understanding the biology,” said Roboz.

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